

BEST AVAILABLE COPY

USSN 10/646,308

Docket No. 3432-B RECEIVED  
CENTRAL FAX CENTER  
MAR 13 2007**Amendments to the Claims**

The listing of claims will replace all prior versions and listings of claims in the application:

1-30 (canceled)

31. (New) A method of treating a cardiovascular disease in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a 4-1BB antagonist, wherein the cardiovascular disease is selected from the group consisting of chronic heart failure, post-pump syndrome, ischemia/reperfusion injury, non-ischemic systemic hypertension, arrhythmogenic valvular disease, ischemic valvular disease, atherosclerosis, arteriosclerosis, peripheral vascular disease, coronary artery disease, stroke, transient ischemic attack, myocardial infarction, aneurysm, arteritis, angina, embolism, platelet-associated ischemic disorders, restenosis, mitral and/or tricuspid regurgitation, mitral stenosis, silent myocardial ischemia, Raynaud's phenomena, thrombosis, pulmonary embolism, thrombotic microangiopathies, vasculitis, veno-occlusive disease, giant cell arteritis, Wegener's granulomatosis, Schoenlein-Henoch purpura, and cardiovascular disease arising from a bacterial periodontal infection.

32. (New) The method of Claim 31, wherein the 4-1BB antagonist is selected from the group consisting of: a soluble 4-1BB; an antibody that specifically binds 4-1BB and blocks the interaction of 4-1BB and 4-1BB-L; and an antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.

33. (New) The method of Claim 32, wherein the 4-1BB antagonist is a soluble 4-1BB, and further wherein the soluble 4-1BB is an Fc fusion protein.

34. (New) The method of Claim 32, wherein the 4-1BB antagonist is an antibody that specifically binds 4-1BB and blocks the interaction of 4-1BB and 4-1BB-L or an antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.

35. (New) The method of Claim 34, wherein the antibody is a monoclonal antibody.

36. (New) The method of Claim 34, wherein the antibody is a human antibody.

37. (New) The method of Claim 36, wherein the antagonist is an antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.

USSN 10/646,308

Docket No. 3432-B

REST AVAILABLE COPY

38. (New) The method of Claim 34, wherein the cardiovascular disease is chronic heart failure.
39. (New) The method of Claim 34, wherein the cardiovascular disease is myocardial infarction.
40. (New) The method of Claim 34, wherein the antibody is a humanized antibody.
41. (New) The method of Claim 32, wherein the antibody is a single-chain antibody.
42. (New) The method of Claim 31, wherein the 4-1BB antagonist is administered intravenously or by subcutaneous injection.
43. (New) The method of Claim 31, wherein the 4-1BB antagonist is administered in combination with one or more compounds selected from the group consisting of non-steroidal anti-inflammatory cytokines; chemotherapeutics; lipid-lowering drugs; blood pressure-regulating drugs; angiotensin-converting enzyme inhibitors; antibiotics; corticosteroids; and peroxisome proliferator-activated receptor ligands.
44. (New) The method of Claim 31, wherein the therapeutically effective amount of the 4-1BB antagonist is an amount sufficient to induce a reduction in ischemic cardiomyopathy in the subject.
45. (New) A method of treating a subject suffering from chronic heart failure comprising administering to the subject a therapeutically effective amount of a 4-1BB-L antagonist comprising an antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L, wherein said antibody is selected from the group consisting of a human antibody and a humanized monoclonal antibody.
46. (New) A method for reducing chronic cardiotoxicity caused by a chemotherapeutic agent in a subject who has received the chemotherapeutic agent, comprising administering to the subject a 4-1BB antagonist in an amount sufficient to reduce the cardiotoxicity.
47. (New) The method according to Claim 46, wherein the cardiotoxicity is selected from the group consisting of arrhythmia, myocarditis, pericarditis, myocardial infarction and cardiomyopathy.

USSN 10/646,308

Docket No. 3432-B

48. (New) The method according to Claim 46, wherein the chemotherapeutic agent is an anthracycline drug that is selected from the group consisting of doxorubicin, daunorubicin, epirubicin, idarubicin and mitroxastrone.
49. (New) The method according to Claim 48, wherein the anthracycline drug is doxorubicin.
50. (New) The method according to Claim 46, wherein the 4-1BB antagonist is selected from the group consisting of a soluble 4-1BB protein, an antibody that specifically binds 4-1BB and blocks the interaction of 4-1BB and 4-1BB-L and an antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.
51. (New) The method of Claim 50, wherein the 4-1BB antagonist is soluble 4-1BB, and further wherein said soluble 4-1BB is an Fc fusion protein.
52. (New) The method of Claim 46, wherein the subject is a cancer patient.
53. (New) The method of Claim 46, wherein the chemotherapeutic agent is selected from the group consisting of amsacrine, busulfan, cisplatin, cyclophosphamide, fluorouracil, Herceptin®, ifosfamide, an interferon, interleukin-2, mitomycin, paclitaxel, vinblastine, vincristine and capecitabine.
54. (New) The method of Claim 46, wherein the therapeutically effective amount of the 4-1BB antagonist is an amount sufficient to reduce apoptosis in cardiac tissue of the subject.
55. (New) A method for reducing chronic cardiotoxicity caused by an anthracycline drug in a patient who has received the anthracycline drug, comprising administering to said patient a human antibody that specifically binds 4-1BB-L in an amount sufficient to reduce the cardiotoxicity.
56. (New) A method for treating cancer in a subject in need thereof, comprising administering to the subject an anthracycline drug in combination with a 4-1BB antagonist, wherein the 4-1BB antagonist is administered in an amount sufficient to reduce a cardiotoxic side effect of the anthracycline drug.
57. (New) The method according to Claim 56, wherein the anthracycline drug is selected from the group consisting of doxorubicin, daunorubicin, epirubicin, idarubicin and mitroxastrone.

USSN 10/646,308

Docket No. 3432-B

58. (New) The method of Claim 56, wherein the 4-1BB antagonist is selected from the group consisting of a soluble 4-1BB protein, an antibody that specifically binds 4-1BB and blocks the interaction of 4-1BB and 4-1BB-L and an antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.

59. (New) The method of Claim 58, wherein the 4-1BB antagonist is a human antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.

60. (New) The method of Claim 58, wherein the 4-1BB antagonist is a soluble 4-1BB protein, and further wherein the soluble 4-1BB protein is an Fc fusion protein.

61. (New) The method of Claim 57, wherein the anthracycline drug is doxorubicin and the 4-1BB antagonist is an antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.

62. (New) A method for treating cancer in a subject who has received an anthracycline drug, comprising administering to said subject a 4-1BB antagonist comprising a human antibody that specifically binds 4-1BB-L and blocks the interaction of 4-1BB and 4-1BB-L.